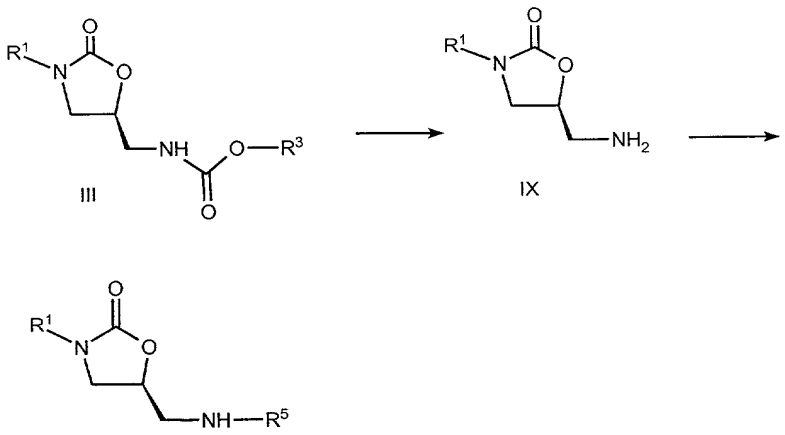
Scheme 7



X, R^5 = C_1-C_6 alkylcarbonyl or C_1-C_6 cycloalkylcarbonyl
XI, R^5 = C_1-C_6 alkylthiocarbonyl or C_1-C_6 cycloalkylthiocarbonyl

to provide a process for the production of an (S)-3,5-disubstituted-oxazolidinone of the structural formula (X) and (XI) which comprises (a) contacting a carbamate of structural formula (I) with an (S)-protected alcohol of formula (V) in the presence of a lithium cation and a base whose conjugate acid has a pKa of greater than about 8 to provide an (S)-protected-oxazolidinone of the structural formula (III) (see Scheme 2), (b) contacting the reaction product of step (a) with aqueous acid to produce an (S)-oxazolidinone free amine of structural formula (IX), and (c) contacting the product of step (b) with a base, such as a tri(C_1-C_5 alkyl)amine, and an acylating or thioacylating agent selected from the group consisting of (i) an acid anhydride of the structural formula $O(R^5)_2$, (ii) an activated acid of the structural formula R^5X to provide (X) or (iii) a dithioester of the structural formula $R^5S(C=S)R^5$ to provide (XI),

wherein R^5 is C_1-C_6 alkylcarbonyl, C_1-C_6 cycloalkylcarbonyl, C_1-C_6 alkylthiocarbonyl, or C_1-C_6 cycloalkylthiocarbonyl, and X is halogen, alkylsulfonyl, or arylsulfonyl.

A further aspect of the present invention is to provide a one pot process for the production of an (S)-oxazolidinone of structural formula (X) and (XI) which comprises (a) contacting a carbamate of formula (I) with either an (S)-t-butylcarbamyl secondary alcohol of the structural formula (IV) or an (S)-t-butylcarbamyl epoxide of the structural formula (II), in the presence of a lithium cation and a base whose conjugate acid has a pKa of greater than about 8, (b) contacting the product of step (a) with aqueous acid, and (c) contacting the reaction product of step (b) with a base, such as a tri(C_1-C_5 alkyl)amine, and and an acylating or thioacylating agent selected from the group consisting of (i) an acid anhydride of the structural formula $O(R^5)_2$, (ii) an activated acid of the structural formula R^5X, or (iii) a dithioester of the structural formula $R^5S(C=S)R^5$, wherein R^5 is C_1-C_6 alkylcarbonyl, C_1-C_6 cycloalkylcarbonyl, C_1-C_6 alkylthiocarbonyl, or C_1-C_6 cycloalkylthiocarbonyl, and X is halogen, alkylsulfonyl, or arylsulfonyl.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

As used herein, the terms and phrases have the meanings, definitions, and explanations known in the art. Some of the more commonly used phrases are described in more detail below.

"Alkyl" refers to a cyclic, branched, or straight chain aliphatic group containing only carbon and hydrogen, for example, methyl, pentyl, and adamantyl. Alkyl groups can be unsubstituted or substituted with one or more substituents, *e.g.*, halogen, alkoxy, acyloxy, amino, hydroxyl, mercapto, carboxy, benzyloxy, aryl, and benzyl. Alkyl groups can be saturated or unsaturated (e.g., containing alkenyl or alkynyl subunits at one or several positions). Typically, alkyl groups contain 1 to about 12 carbon atoms, preferably 1 to about 10, or 1 to about 8 carbon atoms.

"Aryl" refers to a monovalent aromatic carbocyclic group having a single ring (e.g., phenyl), multiple rings (e.g., biphenyl), or multiple condensed rings (e.g., naphthyl or anthryl). Aryl groups can be unsubstituted or substituted with amino, hydroxyl, alkyl, heteroalkyl, alkoxy, halo, mercapto, sulfonyl, nitro, and other substituents. Typically, the aryl group is a substituted single ring compound. For example, the aryl group is a substituted phenyl ring.

The term "halo" or "halogen" is defined herein to include fluorine, bromine, chlorine, and iodine.

The term "alkoxy" and "aryloxy " are defined as -OR, wherein R is alkyl or aryl , respectively.

The term "hydroxy" is defined as -OH.

The term "amino" is defined as $-NR_2$, wherein each R, independently, is alkyl or hydrogen.

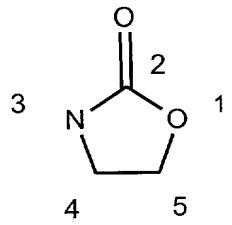
The term "alkylcarbonyl" is defined as R-C(=O)-, where R is alkyl.

The term "alkylthiocarbonyl" is defined as R-C(=S)-, where R is alkyl.

The term "alkylsulfonyl " is defined as $R-SO_3-$, where R is alkyl.

The term "arylsulfonyl " is defined as $R-SO_3-$, where R is aryl.

The oxazolidinone ring system is numbered as follows:



The present invention is directed both to novel synthetic intermediates and to methods of preparing pharmaceutically active and commercially valuable oxazolidinone antibiotics, as defined below by the following general synthetic schemes.